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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,802	08/17/2000	Istvan Boldogh	265.00240101	5387

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/10/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/641,802	BOLDOGH ET AL.	
	Examiner	Art Unit	
	Christopher J. Nichols	1647	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group 37 (Claims 1-15), in part drawn to methods of contacting cells with SEQ ID NO: 2 in Paper No. 8 (17 July 2002) is acknowledged. The traversal is on the ground(s) that examination of Group 37 would not be a burden and that of the 70 groups would require substantial duplication of work on the part of the USPTO. Applicant further argues that the 70-way restriction is a burden for Applicant in terms of filing and maintenance fees. Finally, Applicant argues that Claim 1 is a linking claim and the restriction should have been a requirement to elect a species. Applicant's arguments have been fully considered but are not found to be persuasive. This is not found persuasive because, with regard to Group 37, examination of specific combinations of peptides requires a significant extension of the search required for the elected peptide. It is noted that the claims recite open claims language. Therefore, the elected invention is drawn to methods comprising contacting cells with SEQ ID NO: 2, and the claims embrace methods wherein cells are contacted with generic compositions comprising SEQ ID NO: 2. While the cost to applicant is regretted, the search required for any one peptide recited in the claims is non-coextensive with the search required for any other. Each peptide requires a unique search of the sequence and literature databases. Therefore, an undue search burden is required of the examiner to search all of the peptides together. Finally, regarding Claim 1, it appears that Claim 1 is not a linking claim, since the generic "constituent peptide thereof" does not accurately reflect the Markush group recited in Claim 1, for example. The specifically recited peptides are a subgenus. Since each peptide is structurally unique, restriction was proper. Claims 1-15 will be examined to the extent that they read on methods of

administering SEQ ID NO: 2, active analogs thereof, and generic compositions comprising the peptide SEQ ID NO: 2.

Status of Application, Amendments, and/or Claims

2. The preliminary amendment of 19 June 2001 (Paper No. 5) has been entered in full. The sequence listing has been found to be free of errors and has been entered into the file. Claims 1-15 are under examination.

3. The corrected or substitute drawings were received on 26 February 2001. These drawings are accepted.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code (pp. 9). See MPEP § 608.01.

5. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Specification

Title

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

7. The following title is suggested:

"USE OF A COLOSTRININ, A CONSTITUENT PEPTIDE THEREOF, AND ANALOGS THEREOF, TO PROMOTE NEURONAL CELL DIFFERENTIATION."

8.

9. The specification is objected to because of the following informalities: the following spelling mistakes, "nueral" (pp. 3 line 9) and "terminii" (pp. 8 line 18) and a missing coma between "hydrophobicity and hydrophilicity" (pp. 8 line 24). Appropriate correction is required.

Claim Objections

10. Claims 1-15 are objected to because of the following informalities: claims 1-15 recite non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for promoting neuronal cell differentiation comprising contacting PC12 cells with the peptide of SEQ ID NO: 2 or one active analog thereof which is full-length colostronin, does not reasonably provide enablement for the claimed methods wherein any pluripotent neural cell is differentiated or analogs other than full-length colostronin is administered to cells. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claims 1-8 are directed to methods of promoting cell differentiation in a cell comprising administering SEQ ID NO: 2 or an active analog thereof. Claims 9-13 are directed to methods of promoting neural cell differentiation comprising administering SEQ ID NO: 2 or an active analog thereof to patients, including humans. The specification teaches that full-length colostronin and the peptide SEQ ID NO: 2 have diverse effects when administered to cells or organisms. Specifically, the specification discloses that colostronin and SEQ ID NO: 2 stimulate PC12 cells to differentiate in culture. The prior art teaches that colostronin or an active analog thereof, therein SEQ ID NO: 31, is a polypeptide found in colostrums (Janusz et al. WO 98/14473). The isolated, full-length colostronin and SEQ ID NO: 31 are disclosed as useful in the treatment of disorders of the central nervous system, neurological disorders, mental disorders, dementia, neurodegenerative diseases, Alzheimer's disease, motor neuron disease, psychosis, and neurosis (Janusz et al. WO 98/14473). The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

12. Regarding the scope of pluripotent cells, the art recognizes the enormous range of cells that can be derived from treatment of pluripotent cells with their corresponding regulators and modulators. Due to the large quantity of experimentation necessary to evaluate the effects of SEQ ID NO: 2 on all pluripotent cells, the lack of direction/guidance presented in the specification regarding study of SEQ ID NO: 2's effect on pluripotent cells, the absence of working examples directed to neural pluripotent cells, the complex nature of the invention, the unpredictability of effects any new peptide would have on any pluripotent cells (see Rao, 1999),

and the breadth of the claims which fail to recite limitations which pluripotent cells, especially the expected descent cell types, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

13. Regarding the scope of neural cells, the art recognizes the enormous range of cells that fall under this category, specifically any cells which are derived from the neural crest. Due to the large quantity of experimentation necessary to evaluate the effects of SEQ ID NO: 2 on all neural cells, the lack of direction/guidance presented in the specification regarding study of SEQ ID NO: 2's effect on neural cells, the absence of working examples directed to neural cells, the complex nature of the invention, the unpredictability of effects any new peptide would have on any neural cells (see Schwab, 2002), and the breadth of the claims which fail to recite limitations which neural cells, especially the expected descent cell types, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. Examiner suggests the use of the term, "neuronal", which refers to mature and/or pluripotent cells with characteristics including but not limited to expression of neurofilaments, neuron-like morphology (distinct cell body and processes), and transmission of information via electrical and chemical mechanisms (see Application 09/641,802 FIG 1, "neuron-like").

14. Regarding the scope of analogs; the art recognizes that even minor alterations to protein structure have unpredictable effects on a proteins function. Due to the large quantity of experimentation necessary to all the applicable analogs of SEQ ID NO: 2, the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating non-peptide analogs of SEQ ID NO: 2, the absence of working examples directed to non-peptide analogs of SEQ ID NO: 2, the complex nature of the invention, the unpredictability

of the effects of mutation on protein structure and function (see Ngo et al., 1994 and Wells, 1990), and the breadth of the claims which fail to recite limitations for what constitutes an analog, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

15. Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating non-functional neural cells comprising contacting non-functional neuronal cells, including those in patients, with a neural cell regulator comprising administering the peptide of SEQ ID NO: 2 or one active analog thereof which is full-length colostronin, under conditions effective to convert non-functional neuronal cells to functional neuronal cells when the non-function is the result of neurodegeneration, does not reasonably provide enablement non-functional cells resulting from damage or trauma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claim 14 is directed to methods of treating damaged neural cells comprising contacting nonfunctional neural cells with SEQ ID NO: 2 or an active analog thereof. Claim 15 is directed to methods of treating damaged neural cells in a patient comprising administering SEQ ID NO: 2 or an active analog thereof. The specification teaches that full-length colostronin and the peptide SEQ ID NO: 2 have diverse effects when administered to cells or organisms. Specifically, the specification discloses that colostronin and SEQ ID NO: 2 stimulate PC12 cells to differentiate in culture. The prior art teaches that colostronin or an active analog thereof, therein SEQ ID NO: 31, is a polypeptide found in colostrums (Janusz et al. WO 98/14473). The isolated, full-length colostronin and SEQ ID NO: 31 are disclosed as useful in

the treatment of disorders of the central nervous system, neurological disorders, mental disorders, dementia, neurodegenerative diseases, Alzheimer's disease, motor neuron disease, psychosis, and neurosis (Janusz et al. WO 98/14473). The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

16. Regarding the scope of damaged neural cells; the art recognizes that neural cells, especially those in the central nervous system, when damaged by trauma or injury are recalcitrant to treatment. The adult central nervous system produces specific inhibitory proteins that block neurite outgrowth. This has thwarts any attempt by neural cells near the injury site to differentiate or proliferate (Schawb, 2002). Due to the large quantity of experimentation necessary to all the applicable analogs of SEQ ID NO: 2, the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating non-peptide analogs of SEQ ID NO: 2 in regards to damaged neural cells, such as spinal cord injury, the absence of working examples directed to non-peptide analogs of SEQ ID NO: 2 in use with damaged neural cells, the complex nature of the invention, the unpredictability of the effects therapy on damaged neural cells (see Schwab, 2002), and the breadth of the claims which fail to recite limitations for what constitutes a damaged neural cell, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

17. Claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Janusz et al. (WO 98/1443). Janusz et al. (WO 98/14478) teaches a method of treating damaged neural cells in a patient comprising administering to a patient, colostrinin or an analog thereof, for converting damaged neural cells to functional neural cells in the treatment of disorders of the central nervous system, particularly chronic disorders of the central nervous system including neurological disorders and mental disorders thus meeting the limitation of claims 14 and 15 (pp.2 lines 2-28; pp. 4-6; pp. 9 lines 27-30; pp. 10 lines 1-15). Janusz et al. (WO98/14473) teaches a method comprising administering to a patient with a neurodegenerative disorder such as Parkinson's disease and/or Alzheimer's disease (pp. 2 lines 9-20). Both Parkinson's and Alzheimer's disease represent central nervous system disorders caused by nonfunctional neural cells thus meeting the limitations of Claim 15 (Examples IX and X). In addition, Janusz et al. (WO 98/14473) teaches that colostrinin is characterized by pyschotropic action and hence a therapeutic effect thus meeting the limitations of Claim 15 (pp. 1 lines 28-30; pp. 2 lines 1-10). Therefore, Janusz et al. (WO 98/14473) anticipates Claims 14 and 15.

Conclusion

18. Claims 1-15 are hereby rejected.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, Ph.D. whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D. can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone number for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
September 3, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER